UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,076	05/18/2006	Kathleen D'Halluin	58764.000062	4917

21967 7590 12/11/2007

HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER	
BAGGOT, BRENDAN O	
ART UNIT	**PAPER NUMBER**
1638	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,076	D'HALLUIN ET AL.	
	Examiner	Art Unit	
	Brendan O. Baggot	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-23,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/18/06, 8/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction / Election

1. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/16/07.

2. Claims 1-23 and 31-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Applicant's election with traverse of Group IV, claims 24-30 and SEQ ID NO: 3 in the reply filed on 7/16/07 is acknowledged.

The Applicant traverses on the grounds that the restriction requirement is not consistent with the lack of unity set forth in by the International Searching Authority (see second paragraph on page 20 of the response received on July 16, 2007). this is not persuasive because the USPTO makes its own independent assessment of lack of unity when evaluating claims in a nation stage entry.

The Applicant further traverses on the grounds that Choulika is silent regarding the use of the claimed methods in plant cells and by direct DNA transfer, and that Choulika et al is silent regarding an increase in efficiency when compared with efficiency using *Agrobacterium* mediated DNA delivery (see third paragraph on page 20 of the responses). This is not persuasive, however, because Choulika et al are not silent with regard to using the method in plant cells; they specifically suggest that their method can be used in a plant cell (see paragraph 0052). In addition, Choulika et al is not silent with regard to direct DNA transfer of DNA, in fact, they specifically teach that bombardment or direct uptake can be used to transfer DNA (ese

paragraph 0048). Furthermore, direct transfer of DNA is not required in all of the claims that were restricted (see claims 11, 12, 15-18, and 21-31, in the amendment claim set provided on may 18, 2006). With regard to the relative efficiency compared to *Agrobacterium* –mediated DNA delivery; this is not a limitation in the claims, and therefore it has no bearing on the lack of unity determination.

The Applicant also traverses on the grounds that Choulika does not teach or suggest the limitations of claims 11, 21, and 23 (see fourth paragraph on page 20 of the response). This is not persuasive, however, because in order for a technical feature to be a special technical feature that provides unity of invention, the feature must be present in all the claims. The Applicant is pointing out that claims 11, 21, and 23 have a technical feature that is NOT shared by other claims, therefore, this can not be the special technical feature that provides unity of invention across the claim set.

In addition, the applicant traverses the restriction between Group IV and Groups I-III, because amended claims 5, 11-20, and new claim 32 require sequences of claim 24 (see last paragraph on page 20). This is not persuasive because unity of invention is evaluated across teh entire claim set that was pending at the time of restriction (i.e., the amended claims submitted on May 18, 2006), it is not based on different subsets of claims or claims that are amended subsequent to the restriction requirement being mailed.

However, the Applicant is entitled to rejoinder of methods that depend from or otherwise include all the limitations of a product if the product is found to be allowable. The Applicant is advised that all claims directed to a non-elected process invention must require all the limitations

of an allowable product claim for that process invention to be rejoined.

Notice of Possible Rejoinder

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. The requirement is still deemed proper and is therefore made FINAL.

5. Claims 1-23 and 31-32 are nonelected. Claims 24-30 and SEQ ID NO: 1-4 are examined in the instant application.

Specification

6. The use of the trademark PDS/1000-He Bio Rad biolistic® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. (See page 46).

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112, 1st, paragraph, written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a genus of polynucleotide DNA fragments comprising SEQ ID NO: 2-4 wherein the GC content is 50-60% and wherein the sequence is not SEQ ID NO: 2-4 to the extent set forth in the provisos in claim 25(i-c) or in claim 26(a-cc).

Sufficient description to show possession of such a genus "may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within

the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features.

In this case, Applicants have three sequences of nucleic acids falling within the scope of claims 25-28. These sequences are not representative of the genus of sequences which are not SEQ ID NO: 1-4.

Applicants have NOT described how to make or test sequences other than SEQ ID NOs: 1-4. Because Applicants have not described what domains of those sequences are correlated with the required rare cutting endonuclease activity, and thus have not described which amino acids can be varied according to the claims and still maintain rare cutting activity.

Applicants do not describe sequences which are not SEQ ID NO: 1-4.

No clear depiction of sequences which are not SEQ ID NO: 1-4 is immediately apparent from the specification or claims. No structural features of sequences which are not SEQ ID NO: 1-4 are described. Recitations of what *is not* the claimed subject matter do not render the claimed invention immediately apparent to one of ordinary skill in the art.

The state of the art precludes the artisan from determining which sequences are not SEQ ID NOs: 1-4 and which would have the desired function.

SEQ ID NO: 1-4 are described to be or encode rare cutting restriction endonucleases. The functional characteristics of SEQ ID NO: 1-4 are not correlated with structural features. The artisan would not know what changes could be tolerated while still preserving function. While

the ordinarily skilled artisan can readily make changes, no guidance is provided on which changes to make without ablating enzyme function.

Applicants fail to describe a complete or partial structure of sequences which are not SEQ ID NOs: 1-4 and which have 50-60% GC content and have the desired function.

Applicants fail to describe a representative number of sequences which are not SEQ ID NOs: 1-4 but which have SEQ ID NOs: 1-4 function, have 50-60% GC content and meet the provisos of meet the provisos of claim 25(i-c) or sequences which are not SEQ ID NO: 3 but which have SEQ ID NO: 3 function, have 50-60% GC content and meet the provisos of claim 26(a-cc).

Applicants describe only SEQ ID NO: 2 and 3. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of sequences which are not SEQ ID NO: 2 or SEQ ID NO: 3 and which have 50-60% GC content and have the desired function. Furthermore, given the lack of description of the necessary elements essential for induction of double strand breaks by rare cutting SEQ ID NO: 2 or SEQ ID NO: 3, it remains unclear what features identify sequences which are not SEQ ID NO: 2 but which have SEQ ID NO: 2 function, have 50-60% GC content and meet the provisos of 25(i-c) or sequences which are not SEQ ID NO: 3 but which have SEQ ID NO: 3 function, have 50-60% GC content and meet the provisos of 26(a-cc).

Since the genus of sequences which are not SEQ ID NO: 2 but which have SEQ ID NO: 2 function, have 50-60% GC content and meet the provisos of (i-c) or sequences which are not SEQ ID NO: 3 but which have SEQ ID NO: 3 function, have 50-60% GC content and meet the provisos of (a-cc) has not been described by specific structural features, the specification fails to

provide an adequate written description to support the breath of the claims. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. *See* The Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

Claim Rejections - 35 U.S.C. §112, first paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 24-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 1-4, does not reasonably provide enablement for sequences which meet the limitations of claim 25(i-c) or claim 26(a-cc). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The *Wands* court set forth the enablement balancing test:

> Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *Wands* states at page 1404, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the 'claims."

M.P.E.P. § 2164.01(a).

The claims are broadly drawn to and encompass a multitude of sequences from a multitude of different plant and microbial species. Claim 25 is to a genus of polynucleotide DNA

fragments comprising SEQ ID NO: 2 wherein the GC content is 50-60% and wherein the sequence is not SEQ ID NO: 2 to the extent set forth in the provisos in claim 25(i-c). Claim 26 is to a genus of polynucleotide DNA fragments comprising SEQ ID NO: 3 wherein the GC content is 50-60% and wherein the sequence is not SEQ ID NO: 3 to the extent set forth in the provisos in claim 26(a-cc). Claims 27-29 are to a genus of polynucleotides DNA sequences which differ from SEQ ID NO: 4 by from 0 to 10 positions. SEQ ID NOs: 2-4 are recited to function as a rare cutting endonuclease.

Applicants teach only SEQ ID NOs: 1-4.

Applicants do not teach any polynucleotides comprising SEQ ID NO: 1-4 wherein the GC content is 50-60% and further meeting the provisos in claim 25(i-c) and in claim 26(a-cc) respectively. Applicants do not teach how to determine which limitations recited in claims 25 and 26 are required. Applicants do not teach how to eliminate the many nonfunctional sequences which meet the claimed limitations.

The state-of-the-art is such that one of skill in the art cannot predict which of the sequences within the genus will have the desired function. One of skill in the art would not know which limitation among the many provisos claimed would be required. The Claims amount to an invitation to experiment with SEQ ID NOs: 1-4, mutants and allelic variants. There is abundant prior art to suggest that making substitutions is unpredictable and unsuccessful. Reviews by *Guo* and Lazar detail a variety of problems seen in making substitutions.

While substitutions can be readily made, one of skill in the art would not know which substitutions could be made without inactivating the enzyme. Guo et al, (2004) Protein

Tolerance To Random Amino Acid Change P.N.A.S. 101 (25) 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increase the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Also, Lazar et al (1988, Mol. Cell Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitution with alanine or asparagines had no effect(see abstract). Here Applicant does not even tell what substitutions to make. Applicant only teaches what substitutions to not make. The skilled artisan is left to trial and error experimentation to determine which substituted enzymes will retain the desired function. Here because nucleic acids encode the amino acids discussed in Guo, and because Guo found making changes to amino acids unpredictable, making changes to nucleic acid molecules is also unpredictable.

The specification, while suggesting the use of the SEQ ID NO: 1-4, does not provide significant guidance on how to overcome art recognized problems in enzyme inactivation by random changes to the nucleic acid sequence.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue trial and error experimentation would be required to practice the claimed invention, and therefore the invention is not enabled throughout the broad scope of the claims.

Comment

8. The closest prior art to SEQ ID NO: 1 identified through sequence searches was Dujon, et al., 95.6% identical to SEQ ID NO: 1, found in the Issued Patents Database. Sequence No. 2 from 5474896-A US, issued on 12/12/95.

9. The closest prior art to SEQ ID NO: 2 identified through sequence searches was Dujon, et al., 95.7% identical to SEQ ID NO: 2, found in the Issued Patents Database. Sequence No. 1 from 5474896-A US, issued on 12/12/95.

10. The closest prior art to SEQ ID NO: 3 identified through sequence searches was Dujon, et al., 87.3% identical to SEQ ID NO: 3, found in the Issued Patents Database. Sequence No. 9 from 5474896-A US, issued on 12/12/95.

11. The closest prior art to SEQ ID NO: 4 identified through sequence searches was Dujon, et al., 68.7% identical to SEQ ID NO: 4, found in the Issued Patents Database. Sequence No. 1 from 5474896-A US, issued on 12/12/95.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brendan O. Baggot whose telephone number is 571/272-5265. The examiner can normally be reached on Tuesday through Thursday, 10:00 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571/272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

ANNE MARIE GRUNBERG
SUPERVISORY PATENT EXAMINER